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(54) Title: SELECTED RNA MOTIFS TO INCLUDE CELL DEATH AND/OR APOPTOSIS

(57) Abstract: The present application is directed to the use of dsRNA and/or ssRNA for the purpose of inducing apoptosis or cell death in proliferating cells. Specifically, low molecular weight and high molecular weight dsRNA and ssRNA are shown to induce apoptosis and/or cell death in proliferating cells, to arrest proliferation of transformed cells or tumor cells and to cause rapid induction of the cytokine TNF-alpha and/or also induce production of IL-12 which directs a Th-1 response.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER		
IPC(7) : C12Q 1/68; A01N 43/04; C07H 21/04; A61K 31/07 US CL : 435/6, 91.1, 325, 375; 536/24.3, 24.33, 24.5; 514/44		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/6, 91.1, 325, 375; 536/24.3, 24.33, 24.5; 514/44		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ELBASHIR et al. RNA interference is mediated by 21- and 22-nucleotide RNAs. Genes and Development, 2000 Vol. 15:188-200, see RNA synthesis and cloning of -21 nucleotide RNAs, at page 198.	28-37
X	WIANNY et al. Specific interference with gene function by double-stranded RNA in early mouse development. Nature Cell Biology, 2000 Vol. 2:70-75, see RNA synthesis at page 74.	28-37
A		1-27
X	SVOBODA et al. Selective reduction of dormant maternal mRNAs in mouse oocytes by RNA interference. Development, 2000 Vol. 127:4147-4156, see dsRNA preparation at page 4148.	28-37
X	ZELEZNICK et al. Treatment of leukemic (L-1210) Mice with Double-stranded Polyribonucleotides. Proc Soc Exp Biol Med, 1969, Vol 130:126-128.	1-37
A	BRANCH, AD. A good antisense molecule is hard to find. TIBS, 1998 Vol. 23:45-50, see entire article.	1-27
A	JEN et al. Suppression of gene expression by targeted disruption of messenger RNA: Available options and current strategies. Stem Cells, 2000 Vol. 18:307-319, see entire article.	1-27
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		See patent family annex.
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "B" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed		
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer <i>Mary J. Hale</i> Terra C. Gibbs Telephone No. 571-272-0564

INTERNATIONAL SEARCH REPORTInternational application No:
PCT/US04/09261**C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	OATES et al. Too much interference: Injection of double-stranded RNA has nonspecific effects in the zebrafish embryo. <i>Developmental Biology</i> , 2000 Vol. 224:20-28.	1-27
A	COBURN et al. siRNAs: a new wave of RNA-based therapeutics: <i>Journal of Antimicrobial Chemotherapy</i> , 2003 Vol. 51:753-756.	1-27
A	AGAMI, A. RNAi and related mechanisms and their potential use for therapy. <i>Current Opinion in Chemical Biology</i> , 2002 Vol. 6:829-834.	1-27
A	GREEN et al. Antisense Oligonucleotides: An evolving technology for the modulation of gene expression in human diseases, 2000. <i>J Am Coll Surg</i> Vol. 191:93-105.	1-27
A	AGRAWAL et al. Antisense therapeutics: is it as simple as complementary base recognition? <i>Molecular Medicine Today</i> , 2000 Vol. 61:72-80.	1-27

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Continuation of B. FIELDS SEARCHED Item 3:
CaPlus, EmBase, CancerLit, Medline, NPL, WEST
search terms: double-stranded RNA (dsRNA), single-stranded RNA (ssRNA), short interfering RNA (siRNA)